Clinical Characteristics and Outcomes in Patients With Nosocomial Pneumonia Due to Susceptible, Resistant, and Multidrug-resistant *Pseudomonas aeruginosa*

Poster # 1659

Jean Chastre[1], Catherine Chen[2], Marin H. Kollef[2], Massimo Antonelli[3], Tobias Welte[4], Richard Wunderink[5], Jordi Rello[6], Bernard Clair[7], Helmut Ostermann[8], Esther Calbo[9], Antoni Torres[10], Francesco Menichetti[11], Vandana Menon[12]

[1]Groupe Hospitalier Pitié-Salpêtrière, Paris, France; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]Policlinico Universitario A. Gemelli, Rome, Italy; [4]Medizinische Hochschule Hannover, Hannover, Germany; [5]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [6]Hospital Vall d'Hebron, Barcelona, Spain; [7]Hôpital Raymond-Poincaré, Garches, France; [8]University Hospital of Munich, Munich, Germany; [9]Hospital Universitari Mutúa de Terrassa, Barcelona, Spain; [10]Hospital Clínic de Barcelona, Barcelona, Spain; [11]Cisanello Hospital, Pisa, Italy; [12]Cubist Pharmaceuticals, Lexington, MA, USA

Vandana Menon
Cubist Pharmaceuticals
65 Hayden Ave
Lexington, MA 02421, USA
Tel: (781) 860-8660
E-mail: vandana.menon@cubist.com

BACKGROUND

- Recent trends show an increase in the prevalence of nosocomial pneumonia (NP) caused by multidrug-resistant (MDR) bacteria, most commonly *Pseudomonas aeruginosa* with documented resistance to β-lactams, carbapenems, aminoglycosides, and fluoroquinolones.[1-3]
- The therapeutic effectiveness of current therapies for NP are limited by the increasing prevalence of pathogens that express extended-spectrum β-lactamases (ESBLs), AmpC β-lactamases, or methicillin resistance, emphasizing the need for development of new and effective antimicrobials.
- Initial empirical antibiotic treatment for NP may include the use of cephalosporins, aminoglycosides, fluoroquinolones, penicillins, or carbapenems, alone or in combination. Antibiotic selection is typically individualized based on a given patient's risk factors for MDR pathogens and local susceptibility patterns.
- Prompt and adequate initial antimicrobial therapy has been shown to reduce mortality and improve morbidity associated with NP.[4]

OBJECTIVE

- This international study evaluated characteristics and outcomes of hospitalized patients with NP due to susceptible, resistant, and MDR *P. aeruginosa*.

METHODS

Study Design

- This retrospective multicenter, hospital-based, medical record abstraction study collected data on hospitalized patients with a clinical diagnosis of NP comprising hospital-associated pneumonia (HAP), ventilator-associated pneumonia (VAP), and healthcare-associated pneumonia (HCAP), due to *P. aeruginosa*.
  - HAP was defined as pneumonia that occurred more than 48 hours after admission.
  - VAP was defined as pneumonia that occurred more than 48 hours after endotracheal intubation.
  - HCAP was defined as pneumonia that occurred in patients who were hospitalized in an acute care hospital for 2 or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic.

Participating Sites

- France: Groupe Hospitalier Pitié-Salpêtrière, Hôpital Raymond-Poincaré
- Germany: University Hospital of Munich, Medizinische Hochschule Hannover
- Italy: Policlinico Universitario A. Gemelli, Azienda Ospedaliera Universitaria Pisana
- Spain: Hospital Universitari Mutúa de Terrassa, Hospital Vall d'Hebron, Hospital Clínic de Barcelona
- United States: Barnes-Jewish Hospital, Mayo Clinic, Northwestern Memorial Hospital

Inclusion Criteria

1. Age 18 years or older
2. Admitted for index hospitalization 36 months prior to study initiation at each site
3. Clinical diagnosis of NP defined as findings consistent with pneumonia on chest x-ray or computed topography scan and either temperature >38.3°C or leukocytosis >10,000 cells/mm^3, or both
4. Microbiological cultures (qualitative or quantitative) obtained within the 24-hour period after initiation of antibiotics
5. *P. aeruginosa* organism cultured from a respiratory specimen, including sputum, pleural puncture, flexible bronchoscopy with protected specimen brush, bronchoalveolar fluid, "mini-BAL" (bronchoalveolar lavage) or transbronchial biopsy, and tracheobronchial aspirate in intubated patients

METHODS (cont'd)

Key Variable Definitions

- Susceptibility[5] was as described in medical records based on local laboratory results:
  - Resistant (R) was defined as resistant or intermediate susceptibility to 1 or 2 antibacterial drugs.
  - MDR was defined as resistant or intermediate susceptibility to at least 1 drug in ≥3 anti-pseudomonal classes.
  - All other infections were defined as susceptible (S).
- Appropriate therapy was defined as an antibiotic that was initiated within 24 hours of the diagnosis date and demonstrated in vitro activity.

RESULTS

Table 1. Baseline Characteristics of Patients by *P. aeruginosa* Susceptibility

	Susceptible (n = 221)	Resistant to 1-2 Drug Classes (n = 224)	MDR (n = 215)
Age, y, mean (SD)	62 (15)	61 (16)	53 (17)
Gender, male, n (%)	156 (71)	158 (71)	135 (63)
Location prior to hospitalization, n (%)			
Home	118 (53)	110 (49)	95 (44)
Skilled nursing facility	18 (8)	14 (6)	13 (6)
Long-term care facility	10 (5)	10 (5)	7 (3)
Assisted living	0 (0)	3 (1)	4 (2)
Inpatient rehabilitation	8 (4)	12 (5)	27 (13)
Other	67 (30)	72 (32)	66 (31)
Unknown	0	3 (1)	3 (1)
Coexisting conditions, n/N (%)			
Sepsis	25/201 (12)	36/194 (19)	45/202 (22)
Acute coronary syndrome	37/200 (19)	16/187 (9)	23/198 (12)
Valvular heart disease	35/203 (17)	19/190 (10)	17/196 (9)
Hypertension	105/213 (49)	108/213 (51)	90/207 (43)
Venous thromboembolism	19/204 (9)	11/191 (6)	17/203 (8)
COPD/asthma	49/208 (24)	45/196 (23)	57/200 (29)
Other respiratory disease	47/200 (24)	51/190 (27)	77/195 (39)
Diabetes	59/198 (30)	58/200 (29)	75/198 (38)
Chronic kidney disease	34/196 (17)	55/197 (28)	52/198 (26)
Chronic liver disease	22/192 (11)	30/186 (16)	36/194 (19)
NP category, n (%)			
HAP	57 (26)	40 (18)	48 (22)
HCAP	77 (35)	48 (21)	66 (31)
VAP	87 (39)	136 (61)	101 (47)
Hospitalized in prior 6 months, n/N (%)	115/194 (59)	97/176 (55)	118/197 (60)
Antimicrobials in prior 30 days, n (%)	59 (27)	72 (32)	94 (44)
Admitted to ICU, n (%)	130 (59)	184 (82)	174 (81)

COPD = chronic obstructive pulmonary disease; ICU = intensive care unit.

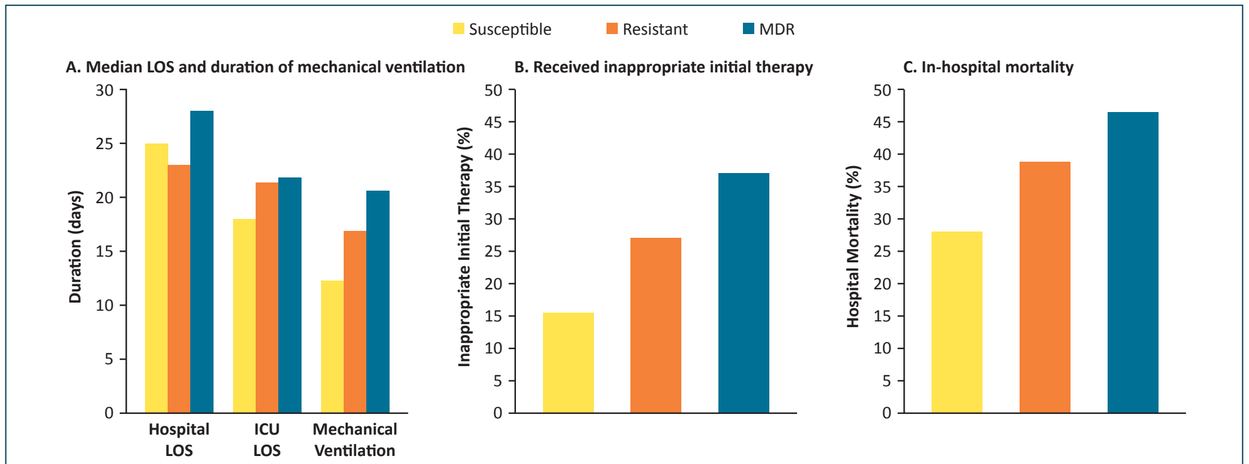
RESULTS (cont'd)

Table 2. Antibiogram by *P. aeruginosa* Susceptibility

		Aminoglycoside	AP-PCN + β-lactamase Inhibitor	Carbapenem	AP Cephalosporin	Fosfomycin	Aztreonam	Ciprofloxacin	Colistin
Susceptible	No. isolates (susceptible %)	221 (100)	218 (100)	217 (100)	219 (100)	44 (100)	92 (100)	218 (100)	97 (100)
Resistant to 1-2 drug classes	No. isolates (susceptible %)	215 (82)	215 (75)	222 (67)	216 (88)	61 (67)	116 (66)	215 (78)	115 (85)
MDR[a]	No. isolates (susceptible %)	215 (29)	210 (21)	215 (15)	215 (28)	86 (41)	157 (14)	211 (22)	154 (97)

[a]Intermediate or resistant to ≥3 antipseudomonal drug classes.
Aminoglycoside: amikacin, gentamicin, tobramycin.
Antipseudomonal penicillin (AP-PCN) + β-lactamase inhibitor: piperacillin/tazobactam, ticarcillin/clavulanate.
Carbapenem: doripenem, imipenem/cilastatin, meropenem.
Antipseudomonal cephalosporin: cefepime, ceftazidime.

Figure 1. Patient Outcomes by *P. aeruginosa* Susceptibility



LOS = length of stay after diagnosis of *P. aeruginosa* NP.

CONCLUSIONS

- The ability for *P. aeruginosa* to develop resistance to multiple classes of antibacterial agents presents a serious challenge.
- There is a strong association between multidrug resistance and inappropriate treatment in NP due to *P. aeruginosa*, and this leads to increased mortality and resource utilization.
- A concerted effort by key stakeholders (healthcare providers and institutions, payers, pharmaceutical companies, policy makers, and regulators) is required to limit further increases in antibiotic resistance and associated societal costs.

REFERENCES

1. Richards MJ, et al. *Crit Care Med*. 1999;27:887-892.
2. Joseph NM, et al. *Eur J Intern Med*. 2010;21:360-368.
3. Rea-Neto A, et al. *Crit Care*. 2008;12:R56.
4. Rello J. *Eur Respir Rev*. 2007;16:33-39.
5. Magiorakos AP, et al. *Clin Microbiol Infect*. 2012;18:268-281.

ACKNOWLEDGMENTS

Editorial and layout support for this poster was provided by PAREXEL and funded by Cubist Pharmaceuticals.

DISCLOSURES

JC has received consulting or lecture fees from Bayer, Pfizer, Basilea Pharmaceutica, Astellas Pharma, Cubist-Trius, and Kenta-Aridis. HO has served as a consultant, and/or speaker and/or received research grants from Astellas, AstraZeneca, Cubist Pharmaceuticals, Gilead, MSD, and Pfizer. MHK has served as a consultant to and/or received research funding from Cubist, Astellas, Pfizer, Forest Laboratories, Cardeas Pharma, the Academy of Infection Management, and Theravance. VM is an employee of Cubist. The remaining authors have no conflicts of interest to report.

This study was funded by Cubist Pharmaceuticals.

Presented at 25th European Congress of Clinical Microbiology and Infectious Diseases

April 25-28, 2015, Copenhagen, Denmark